

### **REMARKS**

Claim 1-34 have been cancelled and claims 35-40 have been added in the present application. The subject matter of claims 6, 7, 27, 33, and 34 is now in new claims 35 – 40, respectively. Claims 35 – 40 will be pending upon entry of this amendment.

Applicants have not introduced any new matter by the amendments. In addition, the amendment does not raise new issues or necessitate the undertaking of any additional search of the art by the Office. All of the elements and their claimed relationships were earlier recited in the claims as examined. As such, Applicants submit that the claim amendments are proper at this stage of prosecution.

Entry of these amendments is respectfully requested.

#### ***Claim Rejections – 35 U.S.C. § 112, first paragraph***

Claims 6, 7, 27, and 33 – 35 (corresponding to present claims 35 – 40) are rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the written description requirement. Applicants respectfully traverse.

#### ***New Matter***

The Examiner contends that the phrase “wherein detecting modification comprises the additional step of quantifying the amount of the inactive MEK or inactive MAPK proteins...” is not supported in the as-filed specification. Office Action, page 2. Specifically, the Examiner contends that the specific modification “phosphorylation” recited in Example 3 is not a support for the broad claimed modification. Applicants point out that “modification” to one or more of the biomolecules is disclosed in at least paragraph [34] on pages 15 and 16. Examples of modifications, including phosphorylation (which is related to kinases) and modifications performed by other enzymes, are disclosed in at least paragraph [124] on pages 58 and 59. Specific examples of proteins being modified, including the MEK proteins, are disclosed in at least paragraph [123] on page 56. As such, “modification” does not constitute new matter, because it is fully supported by the original disclosure.

The Examiner contends that paragraph [0135] does not disclose an inhibitor. In the previous Response dated August 7, 2006, Applicants used paragraph numbers in the published application (US 2002/0028463). Therefore, paragraph [0135] in the published application correspond to paragraph [133] of the application as filed. Applicants point out that inhibitors of the Raf/MEK/MAPK pathway is disclosed in at least Example 3 (including paragraphs [133] and [134]) as well as in Figure 3. Further, inhibitors to pathways in general is are disclosed in at least paragraph [105] on page 47. As such, “inhibitors” does not constitute new matter, because it is fully supported by the original disclosure.

### ***Written Description***

The Examiner contends that the specification fails to provide an adequate written description of how an inactive MEK and MAPK immobilized on a polymer gel mask has been modified simply by exposing it to a solution of active Raf proteins and MEK and potential inhibitors of RAF or active MEK. On pages 4 – 5 of the previous Response, Applicants have explained, and answered the Examiner’s questions in detail regarding how the modification works. Please note that paragraph numbers [0106], [0124], [0135], and [0136] refer to the published application, and the corresponding paragraphs numbers in the as-filed application are [105], [123], [133], and [134], respectively.

The Examiner further contends that it is not apparent from the claims what is being actually claimed, i.e., modification of an inactive immobilized MAPK or MEK, or the different potential inhibitors of the active Raf or MEK.

Applicants point out, again, that independent claim 35 is directed to a method for detecting modification of MEK proteins or MAPK proteins of a Raf/MEK/MAPK pathway. The potential inhibitors are used in the claim method, but are not the claimed subject matter. In the Response dated August 7, 2006, Applicants explained in detail how the claimed method could be used to study potential inhibitors, as disclosed in Example 3 (including paragraphs [133] and [134]) and Figure 3. The explanation was in response to the Examiner’s question regarding inhibitors, not to change the claimed subject matter.

The Examiner contends that the specification does not recite the potential inhibitors that are well known in the art and used specifically for the recited methods. However, the Examiner has not presented arguments as to why the skilled artisan would fail to properly identify the metes and bounds of claim 35. Applicants point out that potential inhibitors, for examples, inhibitors of kinases, are disclosed in paragraph [132] on page 61 and Figure 6. Applicants submit that one of ordinary skill in the art would know what are the potential inhibitors of the pathway in the claimed method. Applicants point out that “potential inhibitors” as recited in the claim are not necessarily true inhibitors that work. In fact, if a potential inhibitor has already been confirmed as an inhibitor of any of the active RAF or active MEK proteins recited in the method prior to the claimed method being performed, then it is not a potential inhibitor anymore. Applicants further point out that the successful performance of the claimed method does not depend on whether the potential inhibitors used in the method turn out to be true inhibitors or not.

For at least the reasons stated above, withdrawal of the rejections is requested.

***Claim Rejections – 35 U.S.C. § 112, second paragraph***

Claims 6, 7, 27, and 33 – 35 (corresponding to present claims 35 – 40) are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particular point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse.

Specifically, the Examiner contends that the step by which the modification of the inactive MEK proteins or MAPK is detected is omitted. Applicants point out that the step of detecting modification of the inactive MEK or MAPK is claimed in step (e) of claim 35. The Examiner contends that simply reciting the term “detecting” without reciting the step as to the modification that occurred such that detection can be made is insufficient and indefinite. Applicants point out that the specific technique of detecting depends on the specific modification, and one of ordinary skill in the art would know what technique to use for a specific modification. Examples of such detecting techniques known in the art are disclosed in at least paragraph [112] on pages 50 and 51. The

specific example of using antibodies to detect modification of proteins is further disclosed in at least paragraph [113] on page 51. Further, the use of antibodies to detect phosphorylated MEK and MAPK is disclosed in paragraph [135]. As stated in the previous Response, phosphorylation is one kind of modification as claimed. Although the claim is not limited to a single modification or detection method, one of ordinary skill in the art, in view of the specification, would appreciate what Applicants are claiming.

The Examiner contends that it is unclear as to the kind, extent and other modifications obtained by the claimed process on the inactive MAPK or MEK immobilized on a substrate. Applicants point out that, as stated in the previous Response, the modification of inactive MEK is caused by active Raf, and the modification of inactive MAPK is caused by active MEK. The extent of modification is the outcome of the claimed method.

The Examiner's contention that Example 3 and the claims contain the same process steps, yet determine different effect(s), is also misplaced. As stated in the previous Response, claim 35 is directed to the method of detecting modification of MEK proteins or MAPK proteins of a Raf/MEK/MAPK pathway. Example 3 discloses an example of how the claimed method is applied to identify inhibitors of the pathway. In Example 3, the phosphorylation of the immobilized proteins was detected through antibody binding. The specific techniques that can be used to in step (e) are disclosed, for example, in Examples 2, 4, and 5. In other words, Example 3 utilized the claimed method by performing steps a) – e), but went further to interpret the results by analyzing the phosphorylation pattern observed. Therefore, Example 3 is consistent with claim 35.

For at least the reasons stated above, withdrawal of the rejections is requested.

***Claim Rejections – 35 U.S.C. § 103, over Duesbery***

Claims 6, 7, 27, and 33 – 35 (corresponding to present claims 35 – 40) are rejected under 35 U.S.C. § 103(a) as allegedly being rendered obvious by Duesbery (US 6,485,925). Applicants respectfully traverse because a *prima facie* case of obviousness has not been established.

To establish a *prima facie* case of obviousness, *inter alia*, the prior art reference must teach or suggest all the claim limitations. M.P.E.P. §2143. Here, many of the limitations of independent claim 35 are not taught or suggested by Duesbery.

As stated in the previous Response, Duesbery simply does not teach or suggest, *inter alia*, “a polymer contact mask having holes” or “immobilizing inactive MEK proteins and inactive MAPK proteins on areas of the substrate underlying the holes.” The Examiner’s contentions that the same effect is achieved by Duesbery and that Applicants have not shown the essentiality or advantages of the contact mask as opposed to Duesbery are simply irrelevant, because the Examiner has not established any motivation to modify Duesbery to include the limitations as recited in claim 35.

For at least the reasons stated above, a *prima facie* case of obviousness has not been established. Withdrawal of the rejections is requested.

***Claim Rejections – 35 U.S.C. § 103, over Ruggieri in view of Mitsuhashi***

Claims 6, 7, 27, and 33 – 35 (corresponding to present claims 35 – 40) are rejected under 35 U.S.C. § 103(a) as being allegedly rendered obvious by Ruggieri (US 6,511,825) in view of Mitsuhashi (WO01/07164). Applicants respectfully traverse because a *prima facie* case of obviousness has not been established.

The Examiner concedes that Ruggieri does not teach immobilizing the kinase to a substrate with a polymer gel contact mask (gasket) in a multiwell plate, but contends that Mitsuhashi discloses a gasket adapted for use with a multiwell microplate.

As pointed out on page 12 in a previous Response dated November 10, 2004, Mitsuhashi does not qualify as prior art under any provisions of 35 U.S.C § 102.

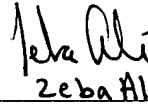
Since Ruggieri does not describe immobilizing the kinase to a substrate with a polymer gel contact mask (gasket) in a multiwell plate, Applicants submit that Ruggieri does not teach each and every element of the claims and therefore a *prima facie* case of obviousness has not been established, and withdrawal of the rejections is requested.

**CONCLUSION**

It is respectfully submitted that the present application is now in condition for allowance, which action is respectfully requested. The Examiner is invited to contact Applicants' representative to discuss any issue that would expedite allowance of the subject application.

Any fees for extension(s) of time or additional fees required in connection with the filing of this response, are hereby petitioned under 37 C.F.R. § 1.136(a), and the Commissioner is authorized to charge any such required fees or to credit any overpayment to Kenyon & Kenyon's Deposit Account No. 11-0600.

Respectfully submitted,  
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